

of the lack of early diagnosis and the small number of cures reflect more adversely upon the doctor previously in charge of the patients than upon the surgeon? Consult the records of Young, Geraghty and Colston of Johns Hopkins, Quinby and Smith of Harvard, Deming of Yale, and many other authorities who are familiar with perineal surgery, for support of Belt's and my attitude toward the treatment of cancer of the prostate. They show operative risks of 4 per cent or less. I know of no publication in support of Bumpus' nihilism, although most urologists, I suspect, practice a similar fatalism—palliation only. Unfortunately, most urologists know nothing about perineal surgery.

Finally, what is accomplished by palliation? (1) X-ray sometimes relieves pain. (2) Radium is a disappointment. (3) Cystotomy is a sign of urologic weakness. (4) Resection removes urinary obstruction, but frequency usually continues, attacks of bleeding are likely to follow, and obstruction commonly recurs. (5) Prostatectomy (partial radical) for urinary obstruction is indicated only when the obstruction is caused by an associated enlargement. It then gives more permanent and greater relief than resection. Whatever method or combination of methods is used, the prolongation of life by palliation has little to commend it either to the public or the profession. At present it is inevitable that palliation in some form be used for the majority. Radical prostatectomy is indicated only when the cancer is so limited that its complete removal seems possible. Naturally, the patient must be in fairly good physical condition. The fact that we see very few patients of this type does not alter the significance of this indication. I am convinced, by reason of my surgical training and urologic experience, that procrastination by the use of palliation is not good practice whenever early cancer is discovered by rectal palpation in a patient otherwise sound who could reasonably withstand surgery.

## SOME INDICATIONS FOR ROENTGEN-RAY TREATMENT

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### PART II\*

#### CHRONIC INFLAMMATIONS

AMONG the chronic inflammations for which roentgenotherapy is indicated are lymphadenitis in any location, and specifically tuberculosis, actinomycosis and blastomycosis. For these conditions larger doses are given, and the treatment is extended over a longer period of time than for acute inflammations. The lymphocytic infiltration in chronic inflammations is not such a prominent feature as in the acute forms; therefore, the mechanism of action of the radiation probably is somewhat different. Considerable connective tissue reaction is present in chronic inflammation, and also usually products of degeneration. Roentgenotherapy will hasten natural reactions and, therefore, shorten convalescence.

On the basis of our experience with the successful roentgen-ray treatment of superficial lymphadenitis, we tried this treatment for patients we had reason to believe had signs and symptoms caused by inflammation and enlargement of the hilar lymph glands. Most of the patients were children who had otherwise unexplainable fever, persistent cough, loss of weight, roentgen evidences of enlarged hilar glands, but without clinical or laboratory evidences of other pathological conditions. Some of them had definite histories of contact with tuberculous indi-

viduals and positive tuberculin reactions; a few had not, but had had previous infections of the upper respiratory tract. Almost every child treated through the mediastinum with small doses of roentgen rays improved promptly, the fever abated, the cough disappeared, and gain in weight and strength soon began. This treatment is not being advocated for pulmonary tuberculosis, but there is no reason why the lymph glands in the mediastinal areas should not become inflamed and cause trouble just as happens in lymph glands in other locations and be just as successfully treated.

It may be said that there are few acute or chronic inflammatory processes that cannot be benefited to some extent by roentgenotherapy, especially if given early. When these conditions are encountered, the tendency is to follow the line of least resistance, to let nature take its course, or follow time-honored procedures. However, in many cases inflammatory processes will be aborted, pain relieved, and the economic usefulness of the patient restored sooner if roentgenotherapy is given promptly.

#### HODGKIN'S DISEASE AND LEUKEMIA

There are some pathologic conditions that have not been proved to be inflammatory or malignant, such as the so-called lymphoblastomas and leukemias. Roentgenotherapy is indicated, and is of benefit in almost every case of this type at some stage in the disease; in fact, it is the only therapeutic procedure that is known to be consistently efficacious.

Hodgkin's disease is a chronic glandular disease which may begin as an acute illness. There often are remissions and exacerbations during its course, but usually it terminates fatally in about three years. Radiologists have differences of opinion about the procedure of treatment of Hodgkin's disease; some advocate irradiation of all gland-bearing areas of the body, whether affected or not, while others direct their attention only to those glands involved. The primary treatment may be fairly intensive, yet should not be too intensive to preclude the possibility of subsequent irradiation for exacerbations which inevitably must develop. There are more and more reports about patients with Hodgkin's disease who have survived five or even more years under treatment, indicating that life is actually prolonged. Of course, all patients have some degree of amelioration of their symptoms, reduction in the enlarged lymph nodes, and extension of their economic usefulness.

The masses of enlarged lymph glands in cases of lymphogenous leukemia disappear with astonishing rapidity, and the abnormal numbers and proportions of white cells in the blood in this disease are brought to normal. Although this disease ultimately is fatal, most patients are made comfortable and their economic usefulness extended. The roentgen-ray treatment should be directed to the affected lymph nodes and spleen, because these structures are primarily affected.

In the myelogenous type of leukemia it is the red bone marrow that suffers damage. The myelocytic series of cells are produced in varying numbers, proportions and stages of maturity, and appear

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in the blood until the red bone marrow, from which they originate, becomes infiltrated and can no longer carry on its erythrocytogenic function; therefore, aplastic anemia ensues from which the patient succumbs. Because of the fact that myelogenous leukemia is a disease that primarily and secondarily affects the red marrow, it is advisable to pay no more attention than necessary to concomitant splenomegaly. The spleen should be irradiated only when and if it is causing discomfort. It is not the cause or origin of the disease, nor does irradiation of it reduce the cell count or benefit the patient to any greater extent than treatment of any organ of equal vascularity as, for example, a lung. Therefore especial attention should be given to the red marrow of the ribs, sternum, vertebrae, and ilia. These bones should be irradiated to preserve their erythrocytogenic function as long as possible and thus delay the development of aplastic anemia.

The acute forms of leukemia are not benefited by roentgenotherapy; in fact, the treatment is contra-indicated.

Dr. Russell Haden and I have been studying the effect of roentgenotherapy for leukopenic leukemia. Patients with cell counts much less than normal have been treated. The treatment has been given cautiously, supportive measures such as transfusions have been employed, and we have observed no ill effects contrary to opinions and warning in the literature. Rather, many patients have improved and, interestingly enough, a few very low white and red cell counts actually have increased.

#### ENDOCRINE DISTURBANCES

One of the newest and most rapidly developing fields for roentgen-ray treatment is the correction of endocrine disturbances.

Hyperthyroidism has been treated, and whether or not this condition is due to dysfunction of the thyroid gland there can be no doubt that irradiation of this organ brings about definite improvement in a satisfactory proportion of cases just as results from thyroidectomy. There are differences of opinion about the indications for irradiation for hyperthyroidism; but I believe that operations performed by especially skilled surgeons are preferable to irradiation because the hyperthyroid state is more promptly relieved. However, if superior surgery is not available or operations are contra-indicated, then roentgenotherapy should be employed. The tendency at present is to give the primary irradiation much more intensely than formerly, thus relieving the symptoms sooner than results from treatment extended over several months. If adequate irradiation is given and improvement does not follow within a reasonable length of time, operations should be performed. Roentgenotherapy given properly by modern techniques will not make subsequent operation more difficult or hazardous.

Roentgenotherapy offers considerable benefit for certain dysfunctions of the pituitary gland in its relationship to other endocrine glands.

Taking into consideration the embryological derivation, anatomy and histology of the anterior lobe of the pituitary, its normal cellular structures

should be radioresistant. However, functions may be altered without demonstrable changes in histology. Some of the indications for roentgenotherapy in connection with endocrine disturbances will be discussed.

The clinical manifestations of excessive amounts of somatotrophic or growth hormone may become apparent either before or after puberty. The effects of this excess upon growth depend upon the time of life when hyperactivity of the anterior lobe of the pituitary begins. If it begins before puberty, or before the epiphyses have united, then abnormal growth, especially of the long bones, may result in symmetrical gigantism with which hypogonadism frequently is associated. If pituitary hyperactivity of this type begins later in life after epiphyseal closure, then the deforming type of skeletal development takes place, which we call acromegaly; and with which hypogonadism usually is associated, as well as other disturbances attributable to pituitary dysfunction, such as goiter with hyperthyroidism, diabetes mellitus, and arterial hypertension.

Only recently irradiating the hypophyses of children with the clinical manifestations of beginning gigantism has been tried, and although treatment offers promise of benefit, we are not prepared to draw conclusions.

The hypophyses in many cases of acromegaly have been irradiated, and we have come to conclusions which may explain the reasons for what have been interpreted as failures of the treatment that we and others have experienced. When acromegaly is in an inactive stage, and when skeletal abnormalities have become established, the deformities of the bones cannot be corrected. Nevertheless, some patients have derived considerable benefit from treatment, extra-ocular palsies have disappeared, headaches abolished, and sexual potency restored. We have been more fortunate in the treatment of acromegaly in its early stages, and believe that we have prevented the progress of skeletal abnormality, corrected other pituitary dysfunctions, and definitely reduced the size of tumors.

Irradiation of the hypophysis, also, has proved to be of value in the treatment of patients who have evidence that the anterior lobe of the pituitary is secreting excessive amounts of gonadotropic hormone due to gonadal deficiency. Excessive amounts of gonadotropic hormone may be associated also with acromegaly in active stages, Cushing's syndrome, or certain types of pituitary tumors. Roentgenotherapy for these conditions is an attack upon pituitary hyperfunction, which is of a compensatory nature such as occurs at the menopause, after castration, or gonadal damage from other causes.

It is well established that, in human beings, excessive amounts of pituitary gonad-stimulating hormones are present in both the blood and urine of males and females, following gonadal deficiency from many causes. These changes accompany the natural menopause and account for positive reactions in assays for prolactin. It has been assumed that, since excessive amounts of gonadotropic hor-

mones are present in the urine under these conditions, it is the excessive prolactin *per se* that is the direct cause of menopausal disturbances. This does not seem logical, because large amounts of prolactin may be present without menopausal disturbances; as, for example, in normal pregnancy, in the presence of hydatiform mole, chorionic epitheliomata, and certain tumors and hyperactive states of the pituitary gland itself. Nevertheless, there is considerable parallelism between the amount of prolactin in the urine and the existence of menopausal disturbances, and they may be reduced effectually by administration of estrin, and a measurable diminution in the amount of urinary prolactin is concomitant with the relief obtained.

When there is an excessive amount of prolactin in the urine in the absence of pregnancy or chorionic tissue, it is presumed to originate from a hyperfunctioning anterior lobe of the pituitary, and represents an excess of the gonadotropic hormone. On this basis it is evident that menopausal disturbances are intimately associated with and probably result from pituitary hyperactivity. Although the mechanism is not clear, the assumption is borne out by the marked improvement that results from roentgen treatment of the hypophysis for menopausal disturbances, whether the symptoms occur naturally or are induced by surgical removal of the gonads, from injury, diseases, or gonadal irradiation. Roentgenotherapy to the hypophysis is especially useful for patients who have been given adequate estrin without relief, or for those who have had repeated recurrences of their disturbances after withdrawal of estrin therapy.

Pituitary hyperfunction also may cause a clinical syndrome which Cushing described and called "pituitary basophilism." The signs and symptoms of this condition will not be described. In some cases, but not all, the condition has been shown to be associated with an increase in the number of basophilic cells in the anterior lobe of the pituitary. It may be that most of the signs and symptoms of Cushing's syndrome are of adrenal origin, because it is well known that adrenal hypertrophy with or without adrenal cortical adenomata is practically a constant finding. That the adrenal may play an important rôle seems particularly plausible because identical clinical manifestations accompany carcinoma and other lesions of the adrenal cortex, and are not associated with increase of the basophilic cellular elements of the pituitary. In spite of good evidence that pituitary basophilism may exist without the clinical manifestations of Cushing's syndrome, it apparently is true that the condition may be attributed to pituitary abnormality in some cases, since most striking benefits often result from roentgen treatment to the hypophysis. In these cases, if the conditions were due to disease primary in the adrenal, the irradiation of the hypophysis could not be so effective.

Bio-assays, such as the Aschheim-Zondek or Friedman test, may be employed to measure any increase in the pituitary gonadotropic hormone, or the amount of prolactin present in the urine which serves as an indication of when the hypophysis

should be irradiated in certain conditions in which there is hyperactivity of the anterior lobe of the pituitary with or without tumor, such as in gonadal deficiencies, acromegaly, and Cushing's syndrome. When excessive amounts of prolactin exist, repeated assays can be used as an index of the degree of depression of the physiologic activity of the pituitary brought about by irradiation. This method may be employed not only to measure the effectiveness of irradiation given for pituitary tumors, but also to give information about the time when excessive glandular activity may recur, thus indicating the necessity for further treatment. Assays of testicular hormone also may be used for men and repeated assays for estrin may be used to advantage for women.

Roentgenotherapy has been found to be particularly efficacious for functional menstrual irregularities which result from ovarian or anterior pituitary lobe dysfunction, and are manifested by amenorrhea or metrorrhagia.

In amenorrhea the menstrual periods sometimes are missed even for months, with a tendency to longer and longer intervals between bleeding or reduced amount of flow with short periods. Apparently both the estrogenic and corpus luteal hormones, which bring about the secretory function of the endometrium, are reduced or lacking. It is thought that the ovary especially is at fault and that this may be due to deficiency in the functions of the anterior lobe of the pituitary. Therefore, two types of amenorrhea are described—the hypopituitary and the hypo-ovarian.

The typical hypopituitary types of individuals are obese, have low metabolic rates, and are sterile. The typical hypo-ovarian types are within normal weight limits, and the basal metabolic rates also are normal, but they are sterile and often complain of many nervous or vasomotor disturbances similar to those of the menopause. However, in milder forms than those that are typical, it may be difficult to distinguish them.

The treatment of these conditions should be carried out under the supervision of a physician familiar with the endocrinological aspects and after complete physical and laboratory examinations, including studies of the endometrium and prolactin and estrogen assays.

For the hypopituitary types, restriction of diet usually is indicated to reduce weight along with administration of thyroid to increase the metabolic rate. When these measures fail, as they may, then small roentgen-ray treatments should be given to the hypophysis.

In the hypo-ovarian type of amenorrhea, the correction of diet and metabolic rate are of minor consideration, because usually there is no indication for interference, but efforts are made to stimulate ovarian activity by various physical methods. Roentgenotherapy in small doses to the ovaries is indicated, and if vasomotor disturbance continues, then the hypophysis may be treated.

It is not at all unusual to have menstrual bleeding take place within a few days after irradiation

of the hypophysis or ovaries for amenorrhea, although when and if ovulation accompanies the bleeding in all cases is doubtful, yet pregnancy may occur promptly in women who have been sterile.

It has been suggested that the small amount of roentgen radiation given in these cases is stimulating. There is no experimental basis for the conclusion. On the other hand, all clinical and laboratory investigations have shown that irradiation is primarily inhibitory, even to the point of complete destruction of cellular function and life. The mechanism of the ovarian or pituitary hormones and their interrelationship are not thoroughly understood. Since all evidence is against the theory that irradiation causes stimulation, it seems most likely that treatment suppresses some hyperactivity, the predominance of which results in hypoactivity of other functions, thus bringing about a return to normal balance.

In the metrorrhagic type of functional menstrual disturbances, the intervals between bleeding are shortened, or they are profuse and prolonged even to the point of continuous bleeding. This condition is thought usually to be due to hyposecretion of only corpus luteal hormones of the ovary; however, there may be an accompanying reduction in urinary excretion of estrogens. Usually metrorrhagia responds to correction of metabolic disturbances, especially of calcium and the administration of pregnancy urine extracts, particularly to young women. However, if bleeding persists, it may be advisable in young women to give very small doses of lightly filtered radium which has a direct effect upon the endometrium without damage to the ovaries. In older women it may be necessary to give sufficient roentgenotherapy to stop menstruation completely.

An interesting metabolic disorder associated with dysfunction of the anterior lobe of the pituitary causes water retention and premenstrual edema. The mechanism has not been satisfactorily explained. Patients with this condition have been normal in weight, but begin to gain suddenly and rapidly for no explainable reason. The weight gain may take place preceding menstruation and be accompanied by severe migraine with evidences of edema of the retina and discs, causing visual disturbances. Proper metabolic measurements will show that it cannot possibly be due to accumulation of fat.

The usual treatment is to begin to restrict the diet very rigidly and to reduce water intake to a minimum. Often remarkable improvement is brought about by intramuscular injections of pregnancy urine extracts and emmenin. But in some cases these measures are unavailing and irradiation then is indicated. For older women approaching the menopause, the quickest and easiest method to correct the difficulty is to stop menstruation by roentgen treatment of the ovaries. Especially grateful are those women who suffer severely from migraine. In young women, irradiation of the hypophysis is beneficial; in fact, often the results are startling. We have seen patients who did not lose weight by diets as low as 500 calories and reduced water intake and who did not respond to

other measures, but lost from ten to twenty pounds within a week or two following moderate irradiation of the pituitary.

It becomes apparent that the best results that are and can be obtained from roentgenotherapy require the closest possible coöperation between physicians and surgeons in all medical specialties and radiologists. The application of roentgenotherapy requires imagination and scientific inquisitiveness, tempered by knowledge of the physical and biological effects of radiation, and of physiology and pathology.

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## CAN CLINICS HELP PRACTITIONERS OF MEDICINE?

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THE answer to this question depends on three considerations: first, the desire of those who operate clinics to help the practicing physician; second, their willingness to do the necessary work to accomplish this desire—for the wish alone is not enough; and third, the eagerness of the practitioner to receive such help.

### THE PROBLEM

In the past, executives and staffs of clinics have had, as their prime and often their only interest, the care of the indigent or near-indigent patient. The latter's problems alone have absorbed their major interests and the funds of the institution. The physician who took care of the patient previously and referred him to the clinic has been dismissed, perhaps with a polite "Thank you." Any interest he had in the patient was ignored. In the practice of medicine, however, a physician often retains his interest in a patient, even though that patient receives attention in a clinic. This interest may be, and often is, a scientific one. Perhaps the disorder is one of particular concern to the physician, who may deeply regret the loss of opportunity to complete the diagnosis and to watch the course. He feels that his chance of following through is likely to be ended, once the patient has become one of the hundreds of clinic "cases." He recognizes that the close and highly desirable doctor-patient relationship is jeopardized. Can we wonder, therefore, that there is often an ill-concealed hostility between the doctors of a community and its clinics?

### THE SOLUTION

What can be done to overcome this attitude? The answer is simple enough. Let clinics be helpful to doctors instead of indifferent or even antagonistic. They can be helpful only by actually seeing the doctor's problems and meeting them fairly. Then, if the desire to be of service to him is present, the rest will be comparatively easy.

### IS APPLICANT ENTITLED TO CARE?

The first means of breaking down disaffection is by asking the physician whether or not, in his judg-